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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,449	04/04/2007	Yow-Pin Lim	61959US(51580)	2106

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EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,449	LIM ET AL.	
	Examiner	Art Unit	
	ANDREW D. KOSAR	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *88,96,98 and 99* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,10,12-15,21,25,27,28,31,40-42,45-48,56,57,77-86 and 101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 May 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/24/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *notice to comply*.

Continuation of Disposition of Claims: Claims pending in the application are 1,2,10,12-15,21,25,27,28,31,40-42,45-48,56,57,77-86,88,96,98,99 and 101.

DETAILED ACTION

Response to Amendments/Arguments

Applicant's amendments and arguments filed February 25, 2010 are acknowledged. Claims 1, 2, 10, 12-15, 21, 25, 27, 28, 31, 40-42, 45-48, 56, 57, 77-86, 88, 96, 98, 99 and 101 are pending. Claims 3-9, 11, 16-20, 22-24, 26, 29, 30, 32-39, 43, 44, 49-55, 58-76, 87, 89-95, 97 and 100 are cancelled. Claims 88, 96, 98 and 99 remain withdrawn for the reasons of record. Claims 1, 2, 10, 12-15, 21, 25, 27, 28, 31, 40-42, 45-48, 56, 57, 77-86 and 101 have been examined on the merits.

The objections to the claims are withdrawn.

Applicant's arguments with respect to the rejection of claims 1, 2, 10, 12-15, 21, 25, 27, 28, 31, 40-42, 45-48, 56, 57, 77-86 and 101 under 35 USC § 103(a) have been considered but are moot in view of the new ground(s) of rejection.

Sequence Compliance

Applicant is advised that the application is not in compliance with 37 CFR §§ 1.821-1.825.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR §§ 1.821- 1.825) in order to effect a complete response to this office action.

Specifically, the specification and drawings contain sequence which do not have sequence identifiers and the specification lacks a CRF, paper copy or statement they are the same. For example, Figure 2 contains a sequence which requires a sequence identifier.

Specification/Drawings

The attempt to incorporate subject matter into this application by reference to GenBank accession numbers (e.g. page 8) is ineffective because GenBank accession numbers are not identifying static sequences, but rather can be amended/changed over time and do not necessarily reflect the sequence contemplated by Applicant.

The drawings and Specification are objected to because they contain sequences which are not accompanied by sequence identifiers (SEQ ID NO), as discussed above.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

Claims 25 and 41 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 25 recites properties inherent in IαI and PαI, and therefore is not further limiting of the independent claim. Claim 41 recites the physiological ranges which are accepted in the art, thus it does not further limit the claim from which it depends.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 10, 12-15, 21, 25, 27, 28, 31, 40-42, 45-48, 56, 57, 77-86 and 101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to IαIp compositions, or methods of making or using, "with a purity of IαIp ranging from about 85% to about 100% pure" (e.g. claim 1). However, the specification indicates that IαIp compositions, "refers to a preparation of IαIp proteins, including IαI and PαI in physiological proportions," (e.g. page 7, lines 15 and 16) or, "may be a mixture of [IαI] and [PαI], wherein the IαI and PαI are present in said mixture in a physiological proportion comprising a light chain of inter-alpha inhibitor protein associated with at least one of three heavy chains H1, H2 and H3." (e.g. page 8, lines 16-19). Thus, is it unclear how one can have a purity of IαIp ranging from about 85% to about 100% pure when the components within the IαIp are not fully defined. IαIp does not describe only IαI and PαI, but rather includes other unidentified proteins, and thus one cannot definitively know the purity of any compound without the elements defined.

Claims 10, 12, 13 and 15 do not limit the method of purifying the IαIp protein, describing the how the plasma is handled prior to the method instantly claimed. Claim 1 is drawn to isolating from a blood plasma fraction, therefore identification of such limitations as the plasma being a side fraction from factor IX purification, or cryosupernatant or cryopoor does not alter the method of using a plasma fraction. Alternatively, the additional description of the plasma

handling prior to the method renders claim 1 confusing as to what is intended to mean 'plasma fraction'.

Furthermore, claim 25 renders the claims confusing, as the molecular weights recited are inherent properties of IαI and PαI, and it is confusing as to what Applicant considers to be IαI and PαI if a dependent claim, which must further limit the claim from which it depends, recites a molecular weight range. IαI has an apparent MW of approximately 220 kDa and PαI has an apparent MW of approximately 150 kDa.

Additionally, claim 41 recites the recognized physiological ranges for PαI and IαI, thus it is confusing, because this is a dependent claim, as to what applicant considers the physiological ranges in the independent claims, if this is a further limitation.

Claims 82 and 83 are confusing, as the claims depend from a method, however they appear to be limitations of a method of isolation.

Claim 86 lacks clear antecedent basis. Claim 85 requires at least 85%, however claim 86 includes the range 'about 85%', which can be +/- some unknown margin, including those below 85%. Alternatively, the claim is confusing because it does not limit claim 85, as the upper limit is always 100%.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 10, 12-15, 21, 25, 27, 28, 31, 40-42, 45-48, 56, 57, 77-80 and 101 are rejected under 35 U.S.C. 102(b) as being anticipated by MICHALSKI (US Patent 5,777,081).

Michalski teaches isolation of a purified ITI fraction, where the plasma fraction used is from human plasma and the side product of Factor IX (e.g. spanning column 1, line 63 to column 2, lines 8). Example I of Michalski details the isolation (spanning column 4, line 28- column 5, line 13). The ITI fraction is obtained from fresh or frozen-thawed plasma subjected to cryoprecipitation to remove FVIII, vWF, fibrinogen and fibronectin (thus being cryopoor). The supernatant is subjected to DEAE-Sepharose, the column is washed to obtain a PCC fraction, which contains the ITI proteins and the fraction is concentrated. The fraction is virally inactivated with TnBP/Tween at 24° C for 6 hours. Next, the fraction is chromatographed on DEAE-Sepharose FF, the column is washed where the 1st fraction removed is the ITI containing fraction. FIX is eluted with increasing salt concentration of the eluent. The ITI fraction is again concentrated and chromatographed on heparin-Sepharose, removing Proteins S and C, which are anticoagulants. The column is washed, removing FX and ITI is then eluted. The resulting eluent is concentrated and ultrafiltered, optionally supplemented with arginine and lysine. The product is sterile filtered, transferred to vials and freeze dried.

Here, the same steps are practiced by Michalski, as instantly claimed and described in the instant examples (e.g. instant example 7), thus it must contain the same components in the same ratios, purity and possess the same activities. Michalski additionally describes the resulting product as higher than 90% pure with a major peak about 220 kDa. Furthermore, claim 31 (for example), is anticipated in that it merely limits the ranges the thermal inactivation is practiced at, however claim 28 contains other alternatives and 31 merely limits that aspect to a subset (e.g., claim 28 is A, B or C and therefore claim 31 is A, B' or C). Further, during the isolation, the composition comprises Proteins C and S, which are "additional therapeutic agents" being

anticoagulants (e.g. claim 77). The final product of Michalski contains salts and amino acids (e.g. claim 46).

With regards to the 'label' and 'instructions', The MPEP states, "Where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art. *In re Ngai*, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004) (Claim at issue was a kit requiring instructions and a buffer agent. The Federal Circuit held that the claim was anticipated by a prior art reference that taught a kit that included instructions and a buffer agent, even though the content of the instructions differed.). *See also In re Gulack*, 703 F.2d 1381, 1385-86, 217 USPQ 401, 404 (Fed. Cir. 1983)("Where the printed matter is not functionally related to the substrate, the printed matter will not distinguish the invention from the prior art in terms of patentability .... [T]he critical question is whether there exists any new and unobvious functional relationship between the printed matter and the substrate.")." (MPEP § 2112.01). Here, the final product is clearly placed into vials, which qualifies as a kit and is intended for use as a therapeutic, thus being 'instructions for use'.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 10, 12-15, 21, 25, 27, 28, 31, 40-42, 45-48, 56, 57, 77-86 and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over MICHALSKI (US Patent 5,777,081), above, in view of LIM (WO 01/632,280 A2).

The teachings of Michalski are presented above. Michalski indicates the composition is for therapeutic use, however Michalski does not specifically indicate what the therapeutic use is. Lim teaches that ITI is useful for treating sepsis (e.g. claim 21). Thus, it would have been obvious to have used the composition of Michalski to treat sepsis, as Michalski teaches the composition is for therapeutic use, and Lim provides a therapeutic use for ITI. One would have been motivated to have used the composition of Michalski, as Michalski teaches the composition is highly purified and sterile, making it optimal for pharmaceutical use. One would have had a reasonable expectation for success in using the composition of Michalski in treating sepsis as, the composition of Michalski is a therapeutic composition and Lim provides the instructions for practicing the method.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the foregoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of

the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANDREW D. KOSAR whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Andrew D Kosar/
Primary Examiner, Art Unit 1654